
Establishing Cerebral Organoids as Models of Human-Specific Brain Evolution.

Journal: Cell

Publication Year: 2019

Authors: Alex A Pollen, Aparna Bhaduri, Madeline G Andrews, Tomasz J Nowakowski, Olivia S Meyerson, Mohammed A Mostajo-Radji, Elizabeth Di Lullo, Beatriz Alvarado, Melanie Bedolli, Max L Dougherty, Ian T Fiddes, Zev N Kronenberg, Joe Shuga, Anne A Leyrat, Jay A West, Marina Bershteyn, Craig B Lowe, Bryan J Pavlovic, Sofie R Salama, David Haussler, Evan E Eichler, Arnold R Kriegstein

PubMed link: 30735633

Funding Grants: Center of Excellence for Stem Cell Genomics - Stanford

Public Summary:

Scientific Abstract:

Direct comparisons of human and non-human primate brains can reveal molecular pathways underlying remarkable specializations of the human brain. However, chimpanzee tissue is inaccessible during neocortical neurogenesis when differences in brain size first appear. To identify human-specific features of cortical development, we leveraged recent innovations that permit generating pluripotent stem cell-derived cerebral organoids from chimpanzee. Despite metabolic differences, organoid models preserve gene regulatory networks related to primary cell types and developmental processes. We further identified 261 differentially expressed genes in human compared to both chimpanzee organoids and macaque cortex, enriched for recent gene duplications, and including multiple regulators of PI3K-AKT-mTOR signaling. We observed increased activation of this pathway in human radial glia, dependent on two receptors upregulated specifically in human: INSR and ITGB8. Our findings establish a platform for systematic analysis of molecular changes contributing to human brain development and evolution.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/establishing-cerebral-organoids-models-human-specific-brain-evolution>